

## AFRL-SA-WP-SR-2011-0002



# INCIDENCE OF TESTICULAR CANCER IN U.S. AIR FORCE ACTIVE DUTY ENLISTED MALE AIRCREW



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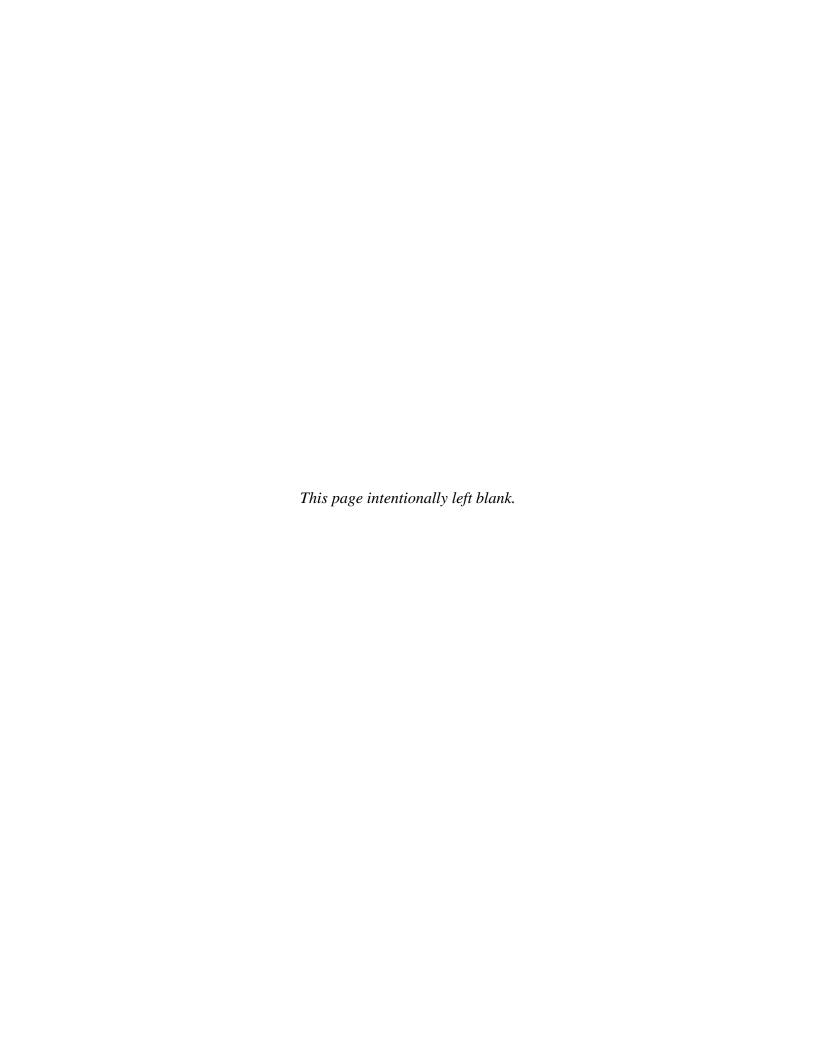
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## TABLE OF CONTENTS

Sectio	on	Page
1.0	SUMMARY	1
2.0	BACKGROUND	1
	2.1 Literature Review  2.2 Aerospace Medicine Significance  2.3 Hypothesis and Research Question	. 3
3.0	METHODS	3
4.0	RESULTS	4
5.0	DISCUSSION	8
6.0	CONCLUSIONS	9
7.0	REFERENCES	9
LIST	OF ACRONYMS	. 11

## LIST OF FIGURES

Figure	e	Page
1	Testicular Cancer Classification	2

## LIST OF TABLES

Table		Page
1	Ages of Study Population	. 4
2	Races of Study Population	. 4
3	Testicular Cancer Incidence (1998-2008)	. 6
4	Testicular Cancer 2x2 Table and Odds Ratio	. 7
5	t-Test	. 8

#### 1.0 SUMMARY

Research studies have provided conflicting results regarding the possible link between flying duties and a higher incidence of testicular cancer. Most of these studies have looked exclusively at pilots or civilian aircrew. No studies to our knowledge have looked at the incidence of testicular cancer in enlisted male aircrew. A retrospective cohort study was conducted using the Automated Central Tumor Registry and Air Force Personnel Center data to determine the incidence of testicular cancer in U.S. Air Force active duty (AFAD) enlisted male aircrew and nonaircrew from 1998 to 2008. There were 13 AFAD enlisted male aircrew and 187 AFAD enlisted male nonaircrew diagnosed with testicular cancer. The sample of AFAD enlisted male nonaircrew had an incidence rate of 7.8 per 100,000, and the sample of AFAD enlisted male aircrew had an incidence rate of 16.6 per 100,000. The odds ratio (2.12) suggested that AFAD enlisted male aircrew had twice the odds of getting testicular cancer than their nonaircrew counterparts. However, a two-tailed t-test on the annual incidence rates revealed that there was no statistical significance between the testicular cancer incidence rates of male aircrew versus male nonaircrew in the AFAD enlisted sample population between 1998 and 2008.

## 2.0 BACKGROUND

#### 2.1 Literature Review

Testicular cancer is a rare condition that has an annual incidence of 5.4 cases in 100,000 males (Ref 1) in the United States. It is, however, the most common cancer in men between the ages of 20 and 34, and the incidence has increased over the past 40 decades (Ref 2). Because much of the male U.S. Air Force (USAF) population is within this age range, this cancer is of significant concern to the USAF. Of all cancers (not including cutaneous basal cell and squamous cell cancers) in USAF active duty (AFAD) males between the period of 1989 and 2009, approximately 18% were testicular cancer (Ref 3). This was the second leading cancer in all AFAD males during that period. Yet, in the U.S. male population, testicular cancer is not among the top 10 leading cancers (Ref 4).

Testicular cancer can be divided into two main categories (see Figure 1). The first category, germ cell tumors, contains 90% of all testicular cancers (Ref 5). Within this first group there are the seminomas, the nonseminomas, and mixed. Leydig and Sertoli cell tumors are examples of the second category, sex chord stromal tumors. Germ cell tumors and sex chord stromal tumors are the majority of primary cancers found in the testes. The World Health Organization adds another nine categories to the above two categories. This "other" group of testicular cancers includes mixed germ/stromal; lymphoid/hematopoietic; tumors of collecting ducts and rete; tumors of tunica, epididymis, spermatic cord, supporting structures, and appendices; soft tissue tumors; secondary tumors; tumor-like lesions; miscellaneous; and unclassified (Ref 6).

The risk factors for testicular cancer are:

- Cryptorchidism
- Personal history of testicular cancer
- Family history of testicular cancer
- Congenital abnormalities

The incidence of testicular cancer seems to be highest in white, tall, Western Europeans (Ref 7).

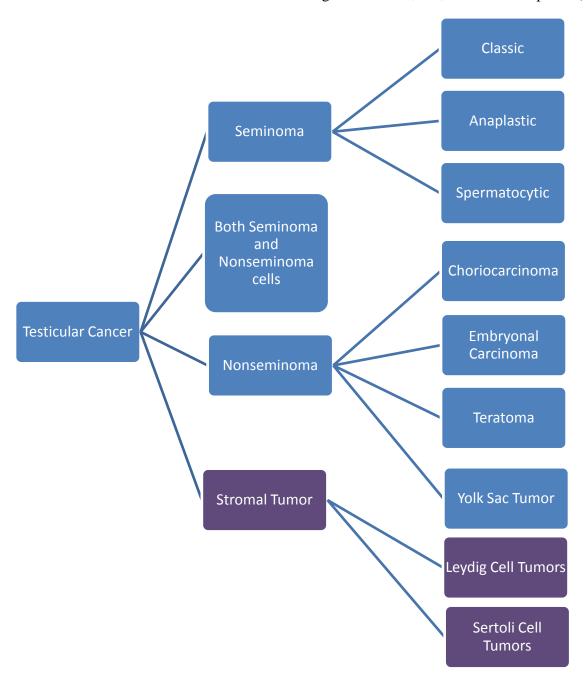


Figure 1. Testicular Cancer Classification (from Ref 8)

Aircrew seem to be at lower risk for cancer overall (Ref 9). However, many studies have found an increased incidence of certain cancers in aircrew. For example, some studies have shown a significant increase in incidence in melanoma and nonmelanoma cancers (Ref 10-12). Testicular cancer is another cancer that has been associated with flying duties. The reasons cited for this possible increase in testicular cancer incidence in aircrew include exposure to higher

doses of cosmic radiation. Aircrew who routinely perform long-haul, high-altitude flights receive an annual radiation exposure between 5 and 9.1 mSievert (mSv) per year, which generally exceeds the recommended annual exposure of 1 mSv (Ref 13). That level of exposure also largely exceeds the average radiation exposure (6 mSv) of an American living at sea level (Ref 14). Whether this increase in radiation exposure is large enough to cause testicular cancer is unknown. Other possible explanations for an increased cancer incidence in aircrew are exposure to sun and exposure to aircraft-generated electromagnetic fields.

Some studies have found an increased incidence in testicular cancer in aircrew, but due mostly to small numbers, the findings were not statistically significant (Ref 11,15). Other studies have failed to find an increased incidence at all (Ref 16). In 2010, a systematic literature review revealed one study that showed a significant increase in testicular cancer incidence in aircrew and five that showed only a slight increase in incidence (Ref 17). The aforementioned studies on testicular cancer in aircrew were conducted in the civilian aviation community, and most were conducted with European populations. One study, however, showed a significant increase in testicular cancer in AFAD male aviators when compared to AFAD male nonflying officers (Ref 18). U.S. military studies looking at testicular cancer incidence in aircrew are rare, and even less common are studies looking at this association with enlisted aircrew. The purpose of this study is to determine if AFAD enlisted male aircrew have a significantly higher incidence of testicular cancer than their nonaircrew counterparts.

## 2.2 Aerospace Medicine Significance

Most studies looking at the incidence of testicular cancer in the flying community have looked at either civilian aircrew (pilots and flight attendants) or pilots exclusively. Additionally, testicular cancer is more common in the higher socioeconomic population. Since Air Force officers have higher incomes than Air Force enlisted personnel, conducting a study that examines AFAD enlisted male airmen explores the possibility that social status may have more to do with the higher incidence of testicular cancer in pilots than does their flying duties. The findings of this study could have an impact on current USAF screening and preventive measures for testicular cancer, thus reducing the incidence, reducing mortality, and saving money in healthcare.

## 2.3 Hypothesis and Research Question

The research question is: "Is the incidence rate of testicular cancer in AFAD enlisted male aircrew significantly higher than in nonaircrew?" The hypothesis is that there is no significant difference in the incidence of testicular cancer between the AFAD enlisted male aircrew population and the AFAD enlisted male nonaircrew population.

## 3.0 METHODS

The study subjects were AFAD enlisted male aircrew and nonaircrew with a diagnosis of testicular cancer. This retrospective cohort study was conducted by the review of extant data and did not require the participation of human or animal subjects. The appropriate Institutional Review Board granted approval for this study. Because the incidence of testicular cancer has increased over the past four decades, inclusion into this study of testicular cancer cases

diagnosed well over a decade ago might skew the results. To reduce the effect of this potential confounder, the study population was limited to cases diagnosed no earlier than 1998. The most recent tumor registry data available for this research study were from 2008. Therefore, the study period is between 1998 and 2008. Raw data were obtained from the following sources:

- Automated Central Tumor Registry (ACTUR)
- Air Force Personnel Center/DSYD division (AFPC/DSYD)
- Interactive Demographic Analysis Systems (IDEAS)

The Armed Forces Institute of Pathology runs ACTUR. This tumor registry was created in 1986 for the purpose of having a centralized Department of Defense data reporting system for cancer cases (Ref 19). Cases of testicular cancer diagnosed from 1988 to 2008 were obtained in the form of an Excel (Microsoft Corp., Redmond, WA) spreadsheet from ACTUR. Only malignant testicular cancer can be reported in ACTUR. Therefore, inclusion of a cancer case in ACTUR with the primary site of involvement being the testis made that case eligible to participate in this study. Histologic distinctions were not made beyond this definition. The resulting ACTUR data originally contained 4,203 cases of testicular cancer. However, 3,106 cases associated with a non-USAF service were removed, including those without a service designation. Of the remaining 1,097 cases, 397 cases of personnel with nonenlisted ranks were removed from the list. Of the remaining 700 cases, 219 duplicate entries were removed. Two cases were removed from the dataset because they contained conflicting information; one case had two different military services and one had an officer rank and an enlisted rank listed. Of the remaining 479 cases, 44 nonactive duty cases were removed. Of the remaining 435 cases, 232 pre-1998 cases were removed from the sample population. The sample population at this point consisted of 203 cases.

ACTUR does not consistently list job descriptions; therefore, AFPC/DSYD supplemented 200 of the 203 ACTUR cases with duty information. Three cases were eliminated from the sample population because AFPC could not find any information on them. For the other 200, Air Force Specialty Codes (AFSCs), Aviation Service Codes (ASCs), and total flying hours were supplied. The enlisted AFSC is a five-character alphanumeric code assigned to a unique job description of USAF enlisted personnel. The ASC is a two-character alphanumeric code that designates flying status. To determine if a member was "aircrew," the presence of any flying hours and/or an assigned ASC as proof of flying duties was used. If neither flying hours nor ASC were present, but a flying-related duty AFSC (denoted by the 1AXXX format) was present, the subject was designated as "aircrew." In one case, neither ASC/flying hours nor a flying-related AFSC was present, but the entry in ACTUR clearly stated "loadmaster," so the subject was included as aircrew. The final sample consisted of 13 aircrew and 187 nonaircrew (200 cases total).

To obtain testicular cancer incidence rates, the entire AFAD enlisted male population had to be quantified. This information was obtained from the IDEAS database, which is available to the public (Ref 20). Using IDEAS, the number of enlisted male aircrew (1AXXX AFSCs) and nonaircrew enlisted personnel (all other AFSCs) for each year from 1998 to 2008 was determined. A filter was used to remove all female personnel data from the final figures. Enlisted personnel without a listed AFSC were not included in the AFAD enlisted population.

A two-by-two table was constructed with the exposure (flying duties) on the y-axis and the outcome (testicular cancer) on the x-axis. Population data were entered into this table and incidence rates were calculated for AFAD enlisted male aircrew and nonaircrew populations. Subsequently, the odds ratio (OR) was calculated. Using Microsoft Excel 2010 Analysis ToolPak (Microsoft Corp., Redmond, WA), a two-tailed t-test was performed to determine if the difference in incident rates was statistically significant.

#### 4.0 RESULTS

There were 200 diagnoses of testicular cancer (n=200) in the AFAD enlisted male population from 1998 to 2008. The mean age was 29. The ages ranged from 18 to 51 (see Table 1). White race accounted for 86% (n=172) of the study subjects (see Table 2); male nonaircrew accounted for 93.5% (n=187) and aircrew accounted for 6.5% (n=13) of the study subjects; and germ cell tumors accounted for 97% (n=194) of the testicular cancer diagnoses, while 1% (n=2) were stromal tumors and 2% (n=4) were not specified. Of the germ cell tumors, seminomas accounted for 54% (n=105), nonseminomas accounted for 18% (n=35), mixed (without mention of the specific cell types) accounted for 25% (n=48), and tumors categorized under the general terms "germ cell tumors" or "germinomas" accounted for 3% (n=6).

Table 1. Ages of Study Population

Age	Aircrewa	Nonaircrewa	Total
Mean	31.54	29.56	29.69
Median	31	28	29
Mode	31	24	27
Minimum	23	18	18
Maximum	41	51	51

<sup>&</sup>lt;sup>a</sup>Total cases=200: aircrew=13, nonaircrew=187.

Table 2. Races of Study Population

Race	Aircrew	Nonaircrew	Total
White	11	161	172
Black	0	5	5
American Indian, Aleutian, or Eskimo	0	1	1
Filipino	0	1	1
Other Asian	0	2	2
Other	1	10	11
Unknown	1	7	8
Total	13	187	200

Of the 11 AFAD enlisted male aircrew, nine were white, one was "other," and one was "unknown." Three were loadmasters, two were cryptologic linguist analysts, two were airborne mission systems specialists, one was an in-flight refueler (boom operator), one was a visual information specialist, one was an aerospace medicine specialist, and two could not be determined with certainty but had a designated ASC and/or had flying hours listed.

Table 3 shows the number of cases and incidence of testicular cancer by year for aircrew and nonaircrew. The "errors" row shows cases that did not have a listed AFSC and were, therefore, not included in the calculations to determine the AFAD enlisted population. Using the calculated incidence rates for each year, an OR of 2.12 was obtained (see Table 4). A confidence interval was not calculated for this OR because the calculations for the OR were based on values that were dependent of each other.

Table 3. Testicular Cancer Incidence (1998-2008)

Group	No. of Cases Population		Ratea	
1998				
Aircrew	1	6,351	15.7	
Nonaircrew	22	230,712	9.5	
Total	23	237,063	9.7	
Errors		983		
Total Enlisted		238,046		
	1999			
Aircrew	0	6,145	0	
Nonaircrew	10	225,345	4.4	
Total	10	231,490	4.3	
Errors		710		
Total Enlisted		232,200		
	2000	<u> </u>	T	
Aircrew	0	5,850	0	
Nonaircrew	21	221,302	9.5	
Total	21	227,152	9.2	
Errors		847		
Total Enlisted		227,999		
- 1	2001			
Aircrew	2	6,552	30.5	
Nonaircrew	19	206,777	9.2	
Total	21	213,329	9.8	
Errors		12,203		
Total Enlisted		225,532		
- 1	2002			
Aircrew	3	6,739	44.5	
Nonaircrew	18	224,963	8.0	
Total	21	231,702	9.1	
Errors		2,861		
Total Enlisted	2002	234,563		
7	2003	7 100	12.0	
Aircrew	1	7,180	13.9	
Nonaircrew	13 14	229,046	5.7	
Total	14	236,226	5.9	
Errors		1,705		
Total Enlisted		237,931		

Table 3. Testicular Cancer Incidence (1998-2008) (concluded)

Group	No. of Cases	Population	Ratea		
2004					
Aircrew	1	7,276	13.7		
Nonaircrew	16	230,130	7.0		
Total	17	237,406	7.2		
Errors		1,473			
Total Enlisted		238,879			
	2005				
Aircrew	0	7,515	0		
Nonaircrew	21	212,595	9.9		
Total	21	220,110	9.5		
Errors		1,099			
Total Enlisted		221,209			
	2006				
Aircrew	4	8,239	48.5		
Nonaircrew	14	209,817	6.7		
Total	18	218,056	8.3		
Errors		977			
Total Enlisted		219,033			
	2007				
Aircrew	0	8,446	0		
Nonaircrew	18	201,836	8.9		
Total	18	210,282	8.6		
Errors		495			
Total Enlisted		210,777			
	2008				
Aircrew	1	8,236	12.1		
Nonaircrew	15	198,276	7.6		
Total	16	206,512	7.7		
Errors		177			
Total Enlisted		206,689			
	Total				
Aircrew	13	78,542	16.6		
Nonaircrew	187	2,390,799	7.8		
Total	200	2,469,328	8.1		
Errors		23,530			
Total Enlisted		2,492,858			

<sup>a</sup>Rate per 100,000.

Table 4. Testicular Cancer 2x2 Table and Odds Ratio<sup>a</sup>

Cancer	Aircrew	Nonaircrew	Total
Yes	13	187	200
No	78,542	2,390,799	2,469,341
Total	78,555	2,390,986	2,469,541

aOR=2.12.

Using a two-tailed t-test (see Table 5), it was determined that the incidence rates of AFAD enlisted male aircrew and those of nonaircrew were not statistically significant. A two-tailed t-test was used because the incidence of testicular cancer could have been higher or lower than the incidence in nonaircrew.

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Statistic	Variable 1	Variable 2
Mean	16.2864	7.846787427
Variance	313.1104	3.124175555
Observations	11	11
Pearson correlation	-0.09121	
Hypothesized mean difference	0	
df	10	
t Stat	1.560024	
P(T<=t) one-tail	0.074907	
t Critical one-tail	1.812461	
P(T<=t) two-tail	0.149815	
t Critical two-tail	2.228139	

<sup>&</sup>lt;sup>a</sup>Paired Two Sample for Means

#### 5.0 DISCUSSION

The incidence of testicular cancer from 1998 to 2008 in AFAD enlisted male aircrew is 16.6 per 100,000, while the incidence in their nonaircrew counterparts is 7.8 per 100,000. However, because of the highly varying incidence of testicular cancer in a year-by-year basis in the aircrew population (ranging from zero to 48.5 per 100,000), there is no significant difference.

This study has several limitations. First, the denominator used to calculate the incidence rate is based on the annual running total of enlisted personnel in the AFAD community. Therefore, many of the AFAD male enlisted personnel counted in one year were counted again in the following year(s). Therefore, these were not independent samples. Another limitation is that age, race, socioeconomic status, and flying hours are potential confounding factors that were not controlled for in this study. Because of the very low incidence of testicular cancer, controlling for age may be difficult unless grouped into age ranges. Controlling for race can be accomplished with the data provided by AFPC; however, it was beyond the scope of this study. AFAD enlisted males were not stratified by the number of flying hours because data on flight hours were frequently missing. Only 54% of the data provided by AFPC reported aircrew flying hours. Further studies should attempt to control for one or all of the above potentially confounding factors.

The study population consisted of 86% white AFAD enlisted male aircrew. The percentages were similarly proportioned in the aircrew (84.6% white) and nonaircrew (86% white) populations. This differs from the percentage of white individuals (69.1%) in the U.S. population in the year 2000 (Ref 21). Therefore, white race is overrepresented in the study population. Care must be taken not to extrapolate the findings of this study to the U.S. population. Further studies in the general aviation community would expand our understanding of the incidence of testicular cancer in aircrew.

#### 6.0 CONCLUSIONS

Within the ADAF enlisted population from 1998-2008, there was no significant difference in the incidence rate of testicular cancer between aircrew and nonaircrew. This finding differs from the findings of other published research studies that suggest a possible link exists between flying duties and testicular cancer. Further research studies are encouraged to investigate this finding and add to the body of knowledge of the risk of testicular cancer in aircrew.

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## LIST OF ACRONYMS

ACTUR Automated Central Tumor Registry

AFAD Air Force Active Duty

AFPC/DSYD Air Force Personnel Center / DSYD division

AFSC Air Force Specialty Code

ASC Aviation Service Code

IDEAS Interactive Demographic Analysis System

OR odds ratio

USAF United States Air Force